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10/723,091	11/25/2003	Jose Remacle	4044.001	7897

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EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	PAPER NUMBER
1639	
MAIL DATE	DELIVERY MODE
11/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/723,091	REMACLE ET AL.	
	Examiner	Art Unit	
	TERESA WESSENDORF	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,7-9 and 11-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-5, 7-9 and 11-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1, 4-5, 7-9 and 11-21 are pending and under examination.

Claim 6 has been cancelled in the amendments of 5/21/07. (Please see the objection to the claim below).

Claim Objections

Claim 6 is objected to because of the following informalities: this claim has been cancelled during the prosecution of the case hence, the status identifier as "previously presented" is incorrect. (Please see page 5 of the REMARKS made on 5/21/07, applicants state that "claims 2-3 and 6 are cancelled herein without prejudice".)

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-5, 7-9 and 11-21, as amended, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Each of the process of claims 1 and 21 contains the same steps. It is unclear whether the method steps result in the production of unstabilized protein as what would appear to be claimed in claim 1. Claim 21 recites the same process steps as claim 1 but results in a stable protein as recited in the preamble. Clarification/explanation is requested/required.

2. In claim 1, there is insufficient antecedent basis of support for "the activity" of the capture protein.

3. Claims 13 and 14 are inconsistent with claim 1. Claim 1 recites a dry condition. Claim 13 recites "air conditions" and claims 14 "an inert gas condition". Also, is "maintained" in claim 1, the same or different concept as "stored" in claims 13 and 14?

4. In claims 16 and 17 the phraseology "all said capture proteins" is inconsistent with amended claim 1 "a protein".

5. Claim 21 step (a) is confusing as to the new claim limitation that the protein is "being present on an array". This is inconsistent with step (b) reaction with the capture protein. Is the protein being present in the array different or the same as the protein in the spotting solution that reacts with the amino group in the array? Clarification/explanation is requested.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC S 103

Claims 1, 4-5, 7-9 and 11-21, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over either Stillman (20030175827) or Decker(GB 2,016,687A) in combination with either Guo(Faming Zhuanli Shenqing Gongkai) or Sandford (US 2003/0134294) and Schultz et al(20040198637) for reasons of record and as reiterated below.

Stillman discloses throughout the patent at e.g., paragraphs [0010]-[0011]:

> …[A] method for producing a thin film dried protein composition comprising making a protein containing solution that is to be dried on a surface, preferably a biologically active protein. The term "biologically active" includes any protein that can participate in a specific binding reaction, (such as antibodies, antibody fragments, antigens, antigen fragments)(capture proteins, as claimed), as well as peptides or enzymes.) The solution is made with a buffer that maintains the surface pH between about 5.0 and 9.0 during solution **drying and with a saccharide in an amount sufficient to stabilize the protein during solution drying**. The solution is then applied to a support having the surface for depositing. Thin film of protein containing solution is allowed to **dry on the support surface under normal pressures**.

Stillman further discloses throughout the patent at e.g., paragraph [0026], referring to FIG. 3:

> A series of compositions were tested including .... antibody protein. The difference amongst the solutions was the saccharide used, namely, glucose, mannitol, xylose, trehalose, maltodextrin, and glucuronic acid. **Spotted and dried solution spots were tested for shelf life, i.e., the retention of biological activity, in this case, a specific binding reaction.** While some saccharides delivered a higher specific signal than others, all delivered a signal at least twice that of the control solution which did not contain any saccharide.

Decker discloses throughout the article at e.g., pages 2 up to 5, an immunoassay method for the detection and determination of antigens and antibodies. The method comprises an indirect application of an antibody or antigen to a solid support. It generally involves the procedure in which the solid support is precoated with antigen or antibody to potentiate the adherence of the antibody or antigen. The reagents consist of a solid support that has been coated either directly or indirectly with an antigen or antibody and stabilized with a sugar coating to impart a storage capability. The percent of sugar e.g., xylitol, mannitol and sorbitol is given in Table II.

Stillman and Decker do not disclose the use of antiseptic as sodium azide and that the protein is covalently linked to the solid support.

Guo discloses throughout the article, e.g., in the abstract a method in which a protein chip with array of 10-10,000 cm-1 and array size of 5-500 consists of the activated carrier and

spotting solution. The spotting solution is composed of probe (such as antigen, antibody…), fucose, antiseptic (such as Na azide) and C2-10 aliphatic polyol. The protein chip is manufactured by spotting the mixture of probe and spotting solution on the activated carrier sheet, and then blocking with bovine serum. The protein chip may be used to detect, recognize, and identify the antigen, antibody, medicine or its receptors, polysaccharide, agglutinin, tissue, or cell. See further, e.g., pages 12-13; paragraph bridging pages 16 and 17.

Sandford discloses at paragraph [0197] that preservatives like azide are effective to retard or prevent microbial proliferation. Sandford discloses at paragraph [0199] that lyoprotectants are effective to reduce or prevent chemical or physical instability of a protein upon lyophilization and storage. Examples of a polyol are trihydric or higher sugar alcohol (e.g., glycerin, erythritol, glycerol, arabitol, xylitol, sorbitol, and mannitol). Sandford also discloses the use of borate buffer.

Schultz et al discloses throughout the patent at e.g., paragraph 0048]:

> Systems for immobilizing polypeptides on a solid support, as well as the resulting solid supports containing the polypeptides, e.g., protein arrays, are provided. **The systems allow one to covalently or non-covalently attach the polypeptides to the solid support in such a manner as to preserve the function of the polypeptides or to regain**

their functionality once attached. The covalent or non-covalent attachment generally does not substantially affect the structure, function, or activity of the polypeptide (e.g., catalytic activity, ability to bind other polypeptides, ability to bind nucleic acids, ability to bind small molecules, 3-D structure, etc.). The protein arrays of the invention are versatile and can be adapted to a variety of protein analysis formats. The arrays find use in a wide variety of applications, including numerous types of screening protocols and any protein analysis where high throughput parallel analysis is desirable.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use azide in the method of either Decker or Stillman as taught by either Sandford or Guo. The advantages taught by Sandford or Guo would provide the motivation to one having ordinary skill in the art as to the known use of azide as a preservative. The use of azide as a preservative is predictable from the teachings of both Sandford and Guo. It would be within the ordinary skill in the art at the time the invention was made to pick the specific saccharide within those any one taught by Guo Decker or Stillman. Furthermore, as taught by Schultz the protein can be covalently or non-covalently link to the array in a manner that preserves its function.

Response to Arguments

Applicants recognize that Guo teaches that alkyl polyalcohol and antiseptic agent can stabilize bioactivity of target probes in liquid state but requires mycose to stabilize the bioactivity of target probes "in the dry-up process or even in dry state". Guo, page 13, second paragraph. As is well known in the art, mycose is a sugar and not a C5 to C7 polyol. Therefore, one of skill in the art would not have been motivated to stabilize a capture probe under dry conditions with a C5 to C7 polyol. Guo does not teach or suggest contacting a C5 to C7 polyol that is between 1 and 5% of a spotting solution. Instead, Guo discloses a stabilized sampler solution that contains 10-50% (v/v) alkyl polyalcohol.

In reply, applicants' arguments with respect to the "target probes" are unclear. Guo does not recite for any **target** probes. The claim C5-C7 is included in the C2-C10 aliphatic polyol taught by Guo. Since Guo encompasses the claimed polyol then Guo would inherently, if not obviously, have provided stability to the dried composition under a dry condition, even in the presence of another sugar as mycose. Applicants' used of the word comprising does not preclude the mycose of Guo. Furthermore, it would be within the ordinary skill in the art at the time the invention was made to determine the proportion or

amount of the compounds/components that are present in a composition. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, i0 USPQ2d 1843 (Fed. Cir.), cert.denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). See MPEP 2144.05.

Applicants state that Stillman does not teach or suggest a method for the production of a protein micro-array with a

selected capture protein, wherein the activity of the capture protein is maintained under dry conditions with a C5 to C7 polyol that is between 1 and 5% of a spotting solution. Stillman also does not teach or suggest a method for stabilizing the tertiary structure of a capture protein of a protein micro-array stored under dry conditions with a C5 to C7 polyol that is between 1 and 5% of a spotting solution. The methods of denaturing proteins disclosed in Stillman teach away from the intended purpose of the present application of maintaining the activity of the capture protein.

In reply attention is drawn to Stillman at e.g., page 1, paragraph 0001]:

> …[A]…method [wherein]….a **thin film of a biologically active protein containing solution to be dried is deposited on the support surface wherein the film also contains a buffer that maintains the surface pH ..during drying under normal pressures and a saccharide in an amount sufficient to stabilize the protein while drying.** An advantage of the present invention is that one can make thin film assay devices, such as proteomic microarrays, using supports that normally would not be useful. (Emphasis supplied).

Contrary to applicants' assertion Stillman is not a teaching away from the claim invention. Rather, is similar in purpose as that claim of drying a protein to stabilize the protein with the saccharide since the surface denatures the proteins as taught Stillman, above.

Stillman teaches the argued 1-5% concentration of the sugar at e.g., paragraph [0018]:

> ….one can also include alkyl alcohols in the protein containing solution prior to drying, either alone or in combination with a surfactant. These alkyl alcohols provide additional stability, possibly by accelerating protein association with the drying surface.. Suitable alkyl alcohols include methanol, ethanol, and propanol at concentrations of up to 15% v/v, preferably about **1%** v/v to about 10% v/v.

Schultz is employed not for the purpose as argued, rather for its teaching that covalent or non-covalent linking of proteins in an array does not affect the proteins activity. (Please see the discussion of Schutz above).

Decker is argued for the same essential reasons as above i.e., the absence of the proportion 1-5% of e.g., mannitol.

The reply above is incorporated herein.

> When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a **predictable variation, § 103 likely bars its patentability.** For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill. When considering obviousness of a combination of known elements, the operative question is thus "whether the improvement is more than the predictable use of prior art elements according to their established functions." KSR International Co. v. Teleflex Inc., 550 USPQ2d 1385 (2007). (Emphasis added).

Accordingly, there is nothing new, unexpected or unpredictable about the claimed method. The steps of producing a stable protein microarray using sugar is well known and had been done in the art at the time of applicants' invention as shown by the combined teachings of the prior art.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA WESSENDORF whose telephone number is (571)272-0812. The examiner can normally be reached on flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TERESA WESSENDORF/
Primary Examiner, Art Unit 1639

Application Number	Application/Control No.	Applicant(s)/Patent under Reexamination	
	10/723,091	REMACLE ET AL.	
	Examiner	Art Unit	
	TERESA WESSENDORF	1639	